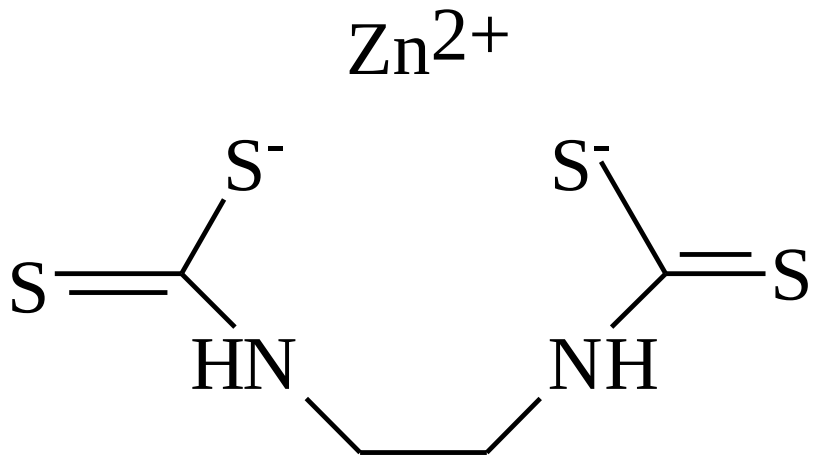
OEHHA

Zineb



Molecular Weight: 275.7

CAS Registry No.: 12122-67-7

Listing History: Zineb

- Listed under Proposition 65 on January 1, 1990
- Originally classified by U.S. EPA as a Group B2 carcinogen (U.S. EPA, 1988)
- Entered into, then dropped from Special Review process
- Never re-classified

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Reviews by Other Authoritative Bodies

- IARC (1976; 1987)
  - Group 3 carcinogen
    - insufficient evidence in animals
    - no human data

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Carcinogenicity Data Available: Zineb

- Mouse sub-chronic oral studies (Chernov and Khitsenko, 1969)
  - Increased lung adenomas in C57BL mice
- Rat long-term oral studies (Mitsumori *et al.*, 1979)
  - Increased thyroid tumors in rats (primarily cystic adenomas)

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Lung Tumors in Mice (Chernov & Khitsenko, 1969)

C57BL mice Lung adenomas	Dose (mg/kg_{bw}) 0	 1750	 3500
High-dose study	0/87		6/79*
Low-dose study	0/59	2/29	

Strain A mice Lung adenomas	Dose (mg/kg_{bw}) 0	 	 3500
High-dose study	30/97		35/101

* Significant increase relative to controls ($p < 0.05$, by Fisher's Exact test)

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Thyroid tumors in rats (Mitsumori *et al.*, 1979)

- Rats (80/sex/group) treated with zineb in diet at 0, 40, 200, 1000, 5000 ppm for 130 weeks
- Increased thyroid tumors in males at 5000 ppm
  - 37.5% treated *vs*. 11.3% controls
  - primarily cystic adenomas
- Increased subcutaneous fibromas in males at 5000 ppm

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Non-positive studies: Zineb

- Mouse oral studies (Innes *et al.*, 1969) - small; less-than-lifetime
- Mouse s.c. injection studies (NTIS, 1968) - small; less-than-lifetime
- Rat gavage and s.c. implant studies (Andrianova & Alekseev, 1970) - poor survival
- Rat oral studies (Blackwell-Smith *et al.*, 1953) - small study

Other Relevant Data: Zineb

Species, strain	Endpoint	Results	Reference
Salmonella typhimurium	Reverse mutation	– –	Croce *et al*., 1995 Franekic *et al*., 1994
Bacillus subtilis	DNA damage Mutation	+ +	Shiau *et al*., 1980 Felkner *et al*., 1981
Saccharomyces cerevisiae	Gene mutation Mitotic chromosome malsegregation	+ +	Franekic *et al*., 1994 Croce *et al*., 1995
Drosophila melanogaster	Genetic damage to somatic and germ cells Mutagenicity	+ –	Tripathy *et al*., 1988 Benes and Sram, 1969
Human peripheral blood lymphocytes	Increased chromosome aberrations	+	Pilinskaya, 1974 (cited in IARC, 1976)

Other Relevant Data: Zineb

- Structural similarity to other ethylene bisdithiocarbamate carcinogens
  (mancozeb, maneb, metiram)

- Metabolized / degraded to ethylene thiourea

Summary: Zineb

- Animal evidence includes benign lung tumors in mice and primarily benign thyroid tumors in rats
- Supporting evidence includes:
  - Some evidence of genotoxicity
  - Structural similarity to known carcinogens
  - Metabolism / degradation to ETU, a known carcinogen, with site concordance